

AMENDMENTS TO THE CLAIMS:

320
Claim 1. (Currently Amended) A ~~foreecasting~~ method of ~~forecasting the pharmacokinetics~~ a pharmacokinetic parameter of a lipid A analog as an aggregate structure in solution or in an injection preparation, wherein said aggregate structure in solution or injection preparation contains ~~containing the a~~ lipid A analog or a pharmacologically acceptable salt thereof, ~~which comprises~~ said method comprising

measuring at least one of membrane fluidity and circular dichroism ~~thereof~~ of the solution or the injection preparation;

preparing a graphical correlation for a plurality of tested lots between the at least one of membrane fluidity and circular dichroism and said pharmacokinetic parameter;


using the measuring of the at least one of membrane fluidity and circular dichroism as well as the graphical correlation to forecast the pharmacokinetic parameter of the solution or the injection preparation.

Claim 2. (Canceled).

Claim 3. (Currently Amended) The ~~foreecasting~~ method according to claim 1, ~~which conducted for~~ wherein quality evaluation is conducted in order to obtain an injection

preparation exhibiting a constant ~~pharmacokinetics~~ pharmacokinetic
parameter.

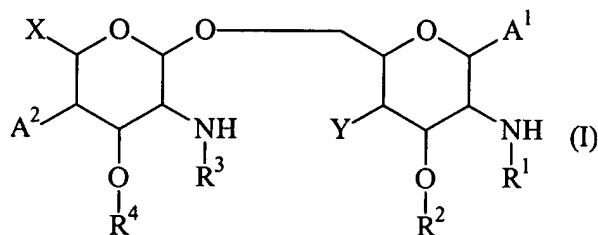
Claim 4. (Currently Amended) The ~~forecasting~~ method according to claim 1, which is conducted ~~in the~~ during preparation ~~step~~ of the injection preparation.

 **Claim 5.** (Currently Amended) The ~~forecasting~~ method according to claim 1, wherein the membrane fluidity is measured by a fluorescence probe method which uses, as parameters, at least one of order parameter (S), fluorescence polarity (P) and fluorescence anisotropy (r).

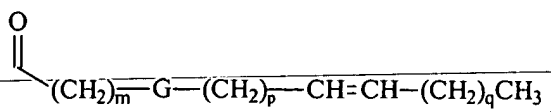
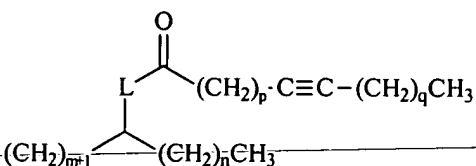
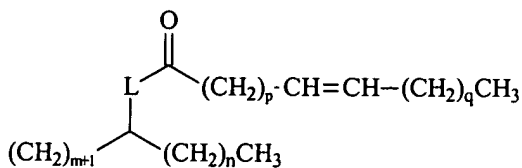
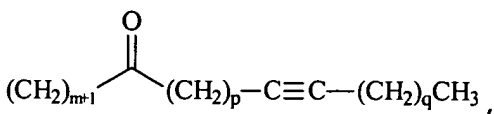
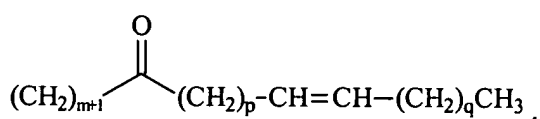
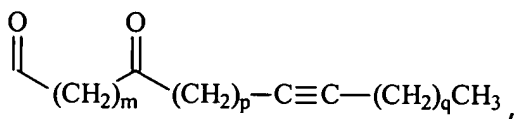
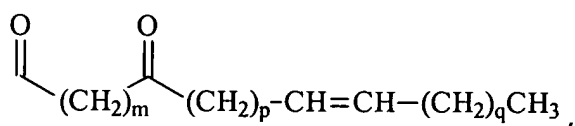
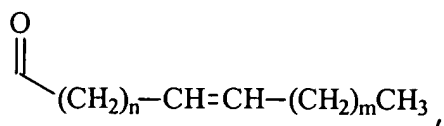
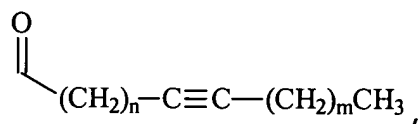
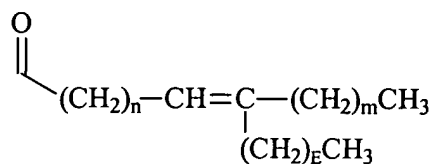
Claim 6. (Currently Amended) The ~~forecasting~~ method according to claim 1, wherein the injection, ~~which~~ preparation further contains aggregates having a diameter not greater than 30 nm, and is prepared by dissolving the lipid A analog or a pharmacologically acceptable salt thereof in an alkaline aqueous solution and then adding a buffer thereto.

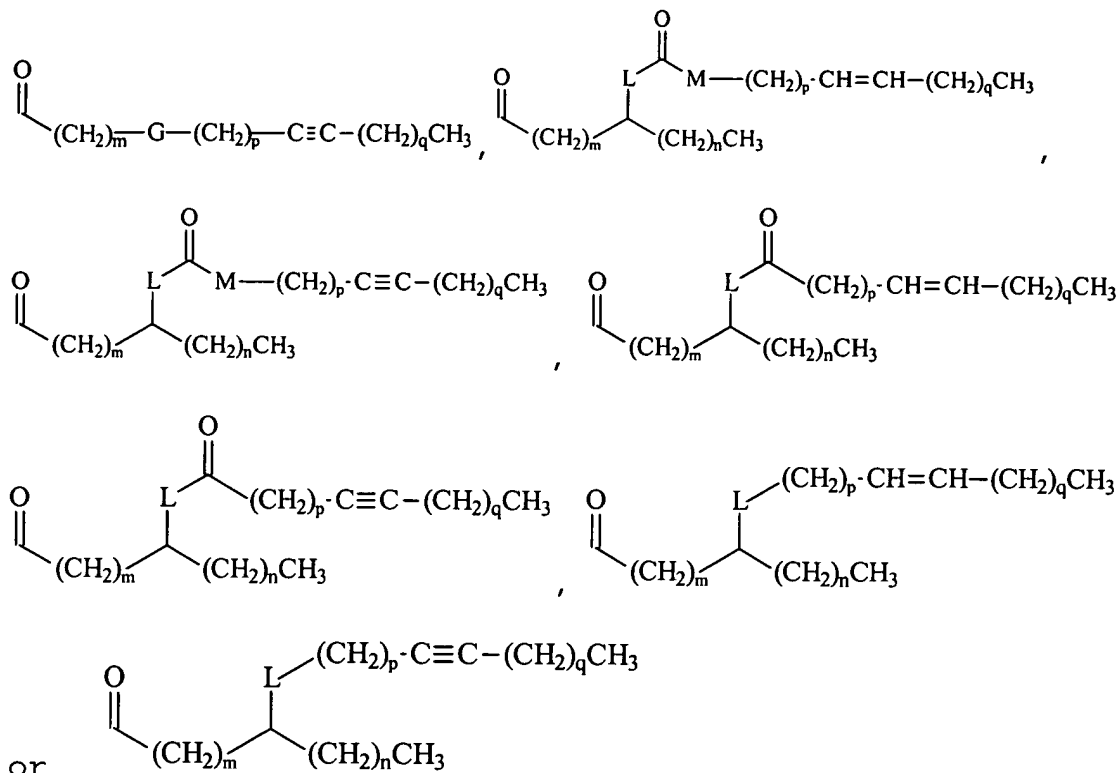
Claim 7. (Currently Amended) The ~~forecasting~~ method according to claim 1, wherein the injection preparation is an aqueous injection or freeze-dried preparation.

Claim 8. (Currently Amended) The ~~forecasting~~ method according to claim 1, wherein the lipid A analog or a pharmacologically acceptable salt thereof is a compound represented by the following formula (I):



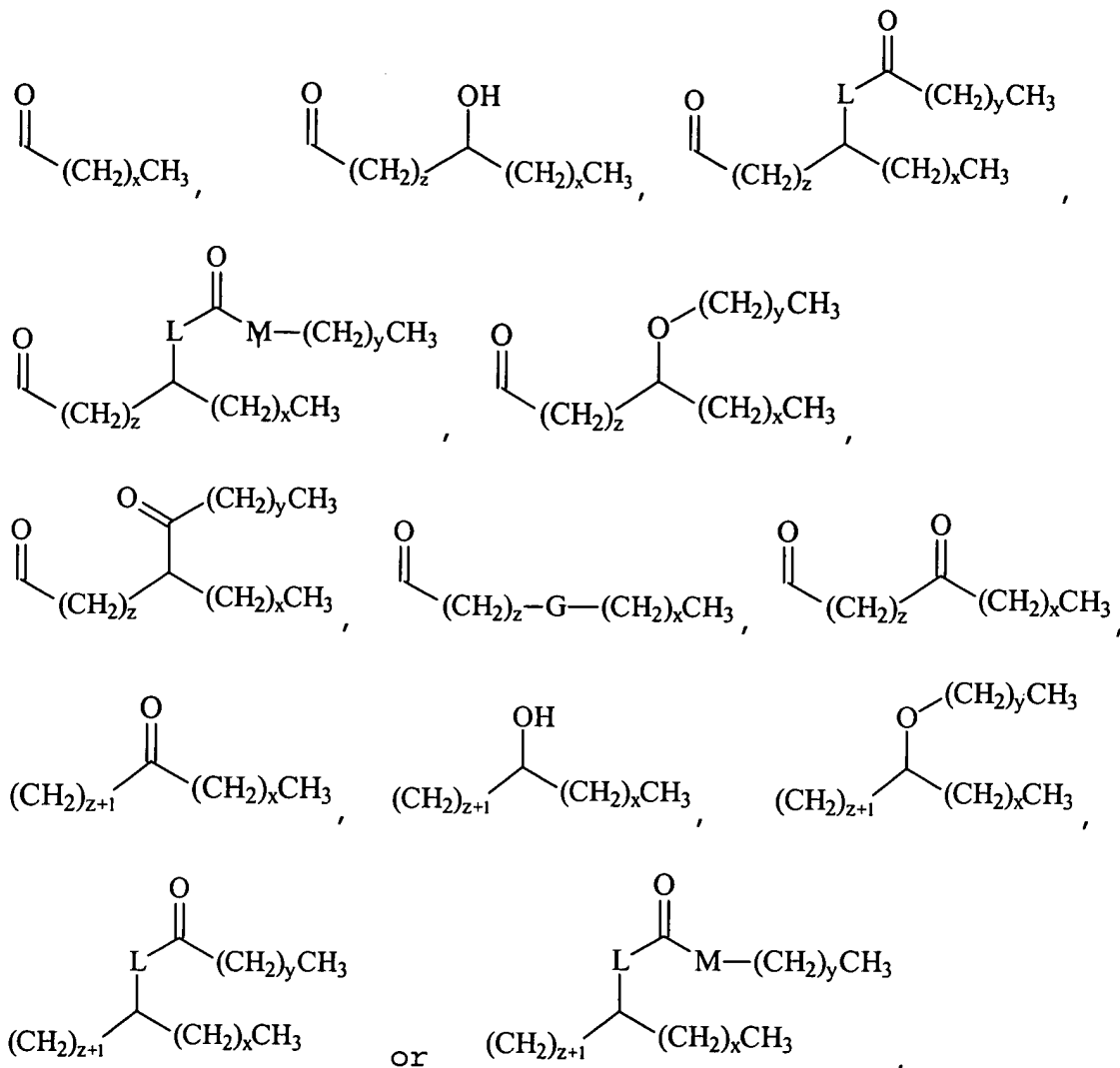
wherein at least one of R^1 , R^2 , R^3 and R^4 is





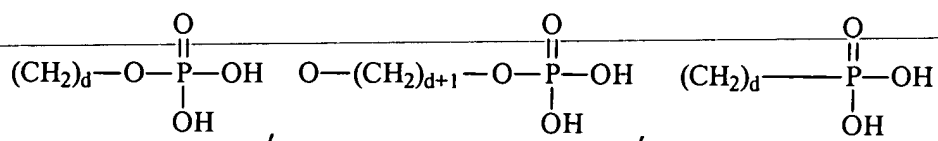
wherein each L is O, N or C; each M is O or N; each E independently is an integer of 0 to 14; each G independently is N, O, S, SO or SO₂; each m independently is an integer of 0 to 14; each n independently is an integer of 0 to 14; each p independently is an integer of 0 to 10; each q independently is an integer of 0 to 10,

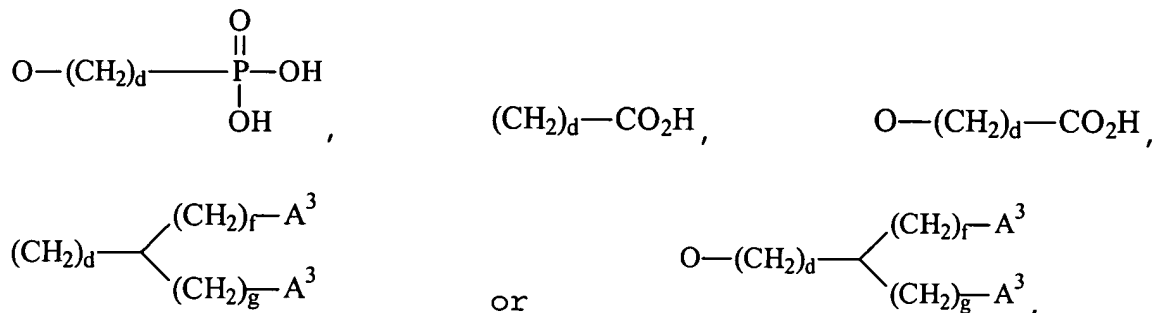
the rest of R¹, R², R³ and R⁴ are, independently of one another,



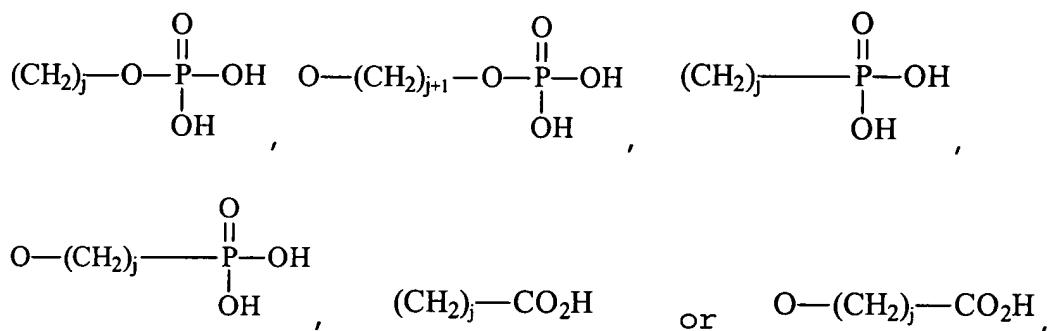
wherein each L is O, N or C; each M is O or N; each x independently is an integer of 0 to 14; each y independently is an integer of 0 to 14; each z independently is an integer of 0 to 10; each G independently is N, O, S, SO or SO₂,

A¹ and A² are, independently of one another, H, OH, OCH₃,



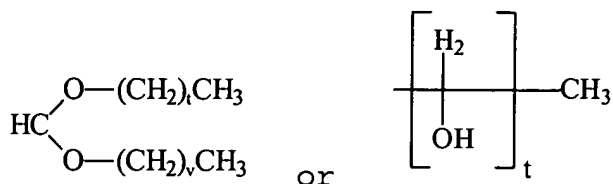


wherein each d independently is an integer of 0 to 5; each f independently is an integer of 0 to 5; each g independently is an integer of 0 to 5; each A^3 independently is



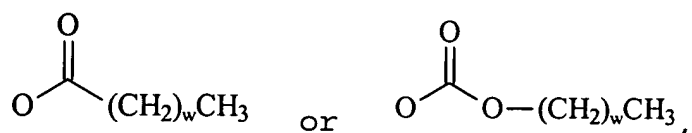
wherein each j independently is an integer of 0 to 14,

X is H , $(\text{CH}_2)_t\text{CH}_3$, $(\text{CH}_2)_t\text{OH}$, $(\text{CH}_2)_t\text{O}(\text{CH}_2)_v\text{CH}_3$, $(\text{CH}_2)_t\text{OPO}(\text{OH})_2$,
 $(\text{CH}_2)_t-\text{CH}=\text{CH}-(\text{CH}_2)_v\text{CH}_3$, $(\text{CH}_2)_t-\text{O}-\text{R}^5$,



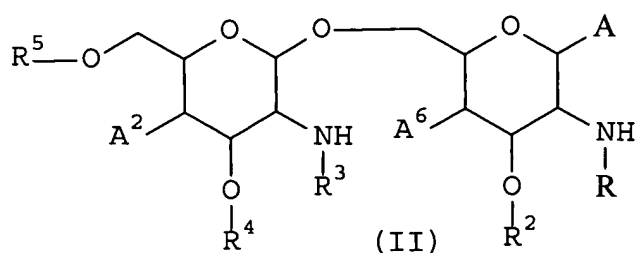
wherein t and v , are independently of one another, an integer of 0 to 14; R^5 is any of the above definitions of R^1 to R^4 ,

Y is H, OH, $O(CH_2)_wCH_3$, a halogen atom,

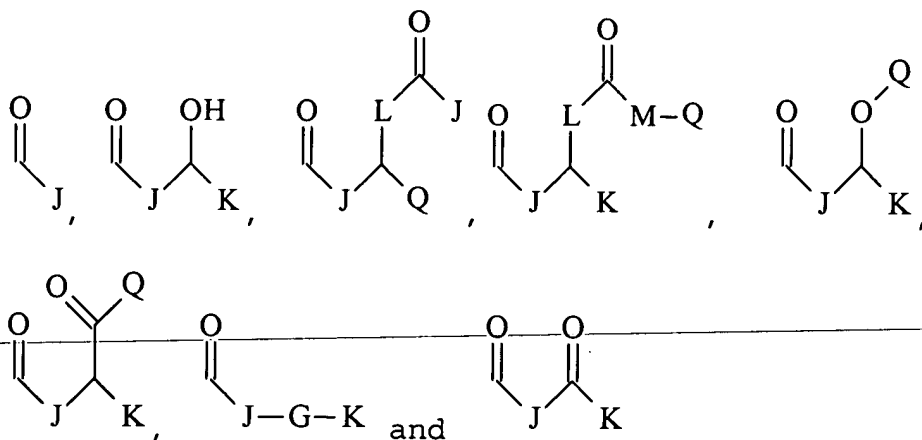


wherein w is an integer of 0 to 14,
or a pharmacologically acceptable salt thereof.

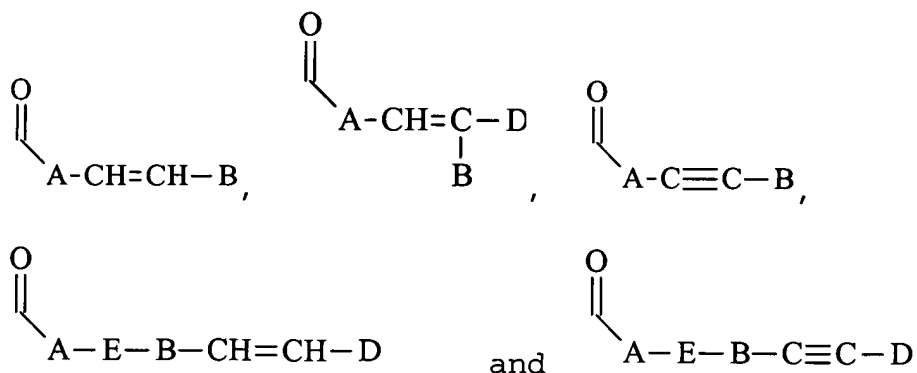
Claim 9. (Currently Amended) The ~~forecasting~~ method according to claim 1, wherein the lipid A analog is a compound represented by the following formula (II):



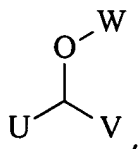
wherein R^1 is a group selected from the groups consisting of



wherein J, K and Q are each a linear or branched alkyl group of 1 to 15 carbon atoms; L is O, NH₂ or CH₂; M is O or NH; G is NH, O, S, SO or SO₂, R² is a linear or branched alkyl group of 5 to 15 carbon atoms, R³ is a group selected from the groups consisting of



wherein E is N, O, S, SO or SO₂; A, B and D are each a linear or branched alkyl group of 1 to 15 carbon atoms, R⁴ is a group selected from the groups consisting of a linear or branched alkyl group of 4 to 20 carbon atoms and



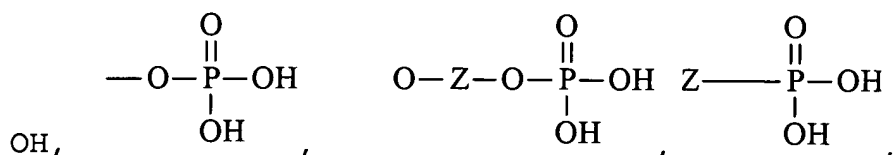
wherein U and V are each a linear or branched alkyl group of 2 to 15 carbon atoms; W is a hydrogen atom or a linear or branched alkyl group of 1 to 5 carbon atoms,

R⁵ is a group selected from the groups consisting of a hydrogen atom, J', -J'-OH, -J'-O-K', -J'-O-K'-OH and

-J'-O-PO(OH)₂, wherein J' and K' are each a linear or branched alkyl group of 1 to 5 carbon atoms,

R⁶ is a group selected from the groups consisting of a hydroxyl group, a halogen atom, an alkoxy group of 1 to 5 carbon atoms, and an acyloxy group of 1 to 5 carbon atoms,

A¹ and A² independently are each a group selected from the groups consisting of

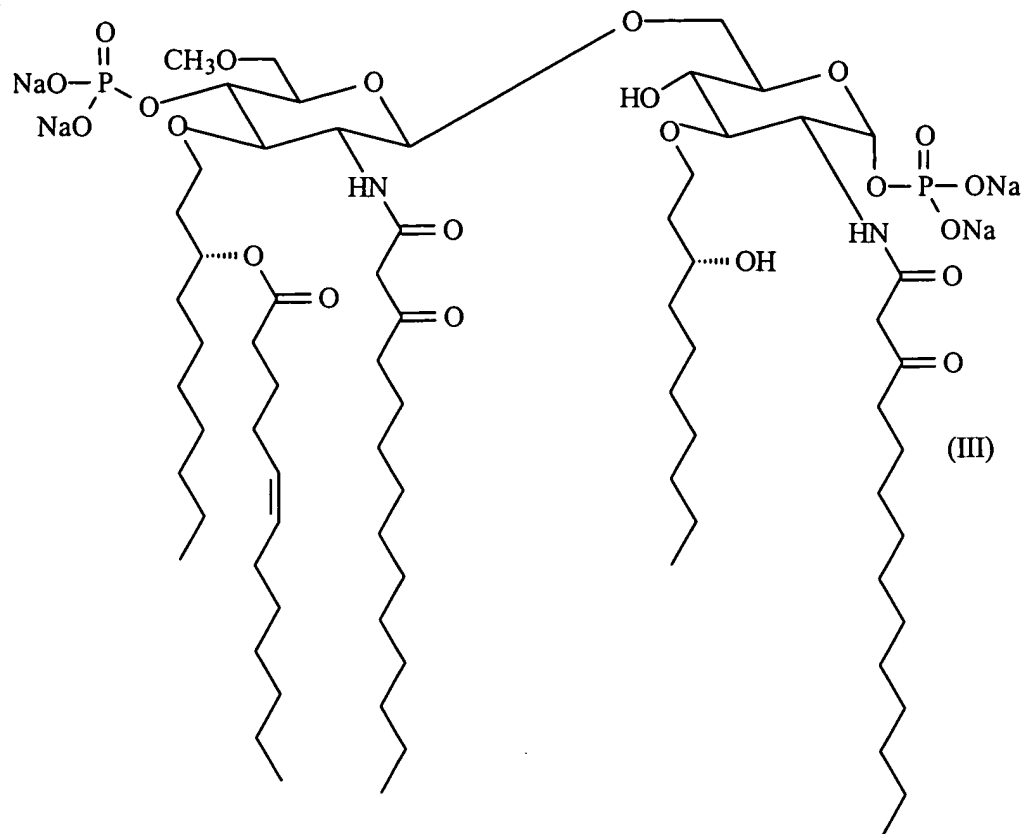


and O-Z-CO₂H,

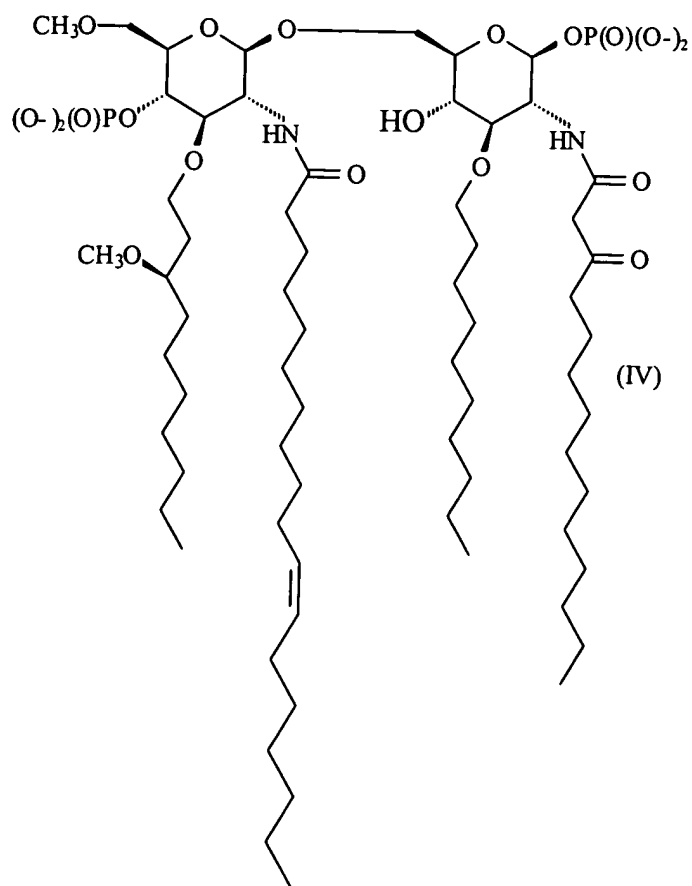
wherein Z is a linear or branched alkyl group of 1 to 10 carbon atoms,

or a pharmacologically acceptable salt thereof.

Claim 10. (Currently Amended) The ~~forecasting~~ method according to claim 1, wherein the lipid A analog is a compound represented by the following formula (III):



Claim 11. (Currently Amended) The ~~foreeasting~~ method according to claim 1, wherein the lipid A analog is a compound represented by the following formula (IV):



028
Claim 12. (Currently Amended) The ~~forecasting~~ method according to claim 1, wherein the lipid A analog or a pharmacologically acceptable salt thereof has an aggregate structure in ~~the form of~~ endoplasmic reticulum ~~with~~ of lipid biomolecular membrane or micelle.